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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/865,022	05/24/2001	Robert P. Hebbel	600.449US1	3307
21186	7590	01/15/2004	EXAMINER	
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A. P.O. BOX 2938 MINNEAPOLIS, MN 55402			NGUYEN, QUANG	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 01/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/865,022

Applicant(s)

HEBBEL ET AL.

Examiner

Quang Nguyen, Ph.D.

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 and 45-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-14 and 45-47 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other:

### **DETAILED ACTION**

Applicants' amendment filed on 11/12/03 has been entered.

Claims 1-14, 45-46 and 47 are pending in the present application, and they are examined on the merits herein.

#### ***Response to Applicants' amendment***

The prior art rejections of record are withdrawn in light of the granted petition for priority claim benefit.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 and 45-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A process for expanding a population of endothelial cells obtained from peripheral blood comprising culturing, in contact with a collagen I-coated surface, mononuclear cells from a buffy coat layer which are obtained from peripheral mammalian blood, in the presence of a cell culture medium containing an effective amount of vascular endothelial growth factor (VEGF), and which medium is free of bovine brain extract, so as to expand the population of endothelial cells from said buffer coat mononuclear cells,

does not reasonably provide enablement for a process for expanding a population of endothelial cells obtained from peripheral blood using any buffer coat cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. **This is a new ground of rejection.**

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

The claims are drawn to a process for expanding a population of endothelial cells obtained from peripheral blood comprising, culturing in contact with a collagen I-coated surface, buffy coat cells which are obtained from peripheral mammalian blood, in the presence of a cell culture medium containing an effective amount of vascular endothelial growth factor (VEGF) and which medium is free of bovine brain extract, so as to expand the population of endothelial cells in said buffy coat cells.

The instant specification is not enabled for the present broadly claimed invention for the following reasons.

**(1) The breadth of the claims.** The claims encompass a process for expanding a population of endothelial cells obtained from peripheral blood by culturing any buffy coat cells, not necessarily limited to buffer coat mononuclear cells, which are

obtained from peripheral mammalian blood in contact with a collagen I-coated surface in the presence of a cell culture medium containing an effective amount of VEGF, and which medium is free of bovine brain extract, so as to expand the population of endothelial cells in said buffy coat cells.

**(2) The state of the prior art and the unpredictability of the prior art.** At about the effective filing date of the present application, endothelial cell populations have been expanded in culture using isolated CD34+ mononuclear cells which are obtained from bone marrow or peripheral blood, including mononuclear cells taken from a "buffy coat" fraction of a peripheral blood sample as taught by Asahara et al. (Science 275:964-967, 1997; Cited previously); Shi et al. (Blood, Vol. 92:362-367, 1998; IDS) and Dzau et al. (U.S. 6,352,555; Cited previously). Additionally, it is well recognized that the physiological art is unpredictable, particularly the differentiation and proliferation of any peripheral blood cell population or any buffy coat cells into endothelial cells in cultures for this instance. This unpredictability is partially supported by the uncertainty of the origin of cells that give rise to endothelial cells lining the impervious Dacron grafts for a long period of time (Shi et al., see background on page 362).

**(3) The amount of direction or guidance provided.** Apart from the disclosure of expanding a population of endothelial cells in culture using buffy coat mononuclear cells, the instant specification fails to provide sufficient guidance, including any example, for a skilled artisan on how to attain an expanding endothelial cell population from any buffy coat cell population, which is not necessarily limited to buffy

coat mononuclear cells. Since the prior art at the effective filing date of the present application does not provide any guidance on the expansion of endothelial cells in culture from non-buffy coat mononuclear cells, it is incumbent upon the present application to do so. With the lack of sufficient guidance provided by the present application, it would have required undue experimentation for a skilled artisan to make and use the process as broadly claimed.

Accordingly, due to the lack of sufficient guidance provided by the specification regarding to the issue set forth above, the unpredictability of the physiological art, particularly the differentiation of any buffy coat cells into endothelial cells, and the breadth of the claims, it would have required undue experimentation for one skilled in the art to make and use the instant broadly claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 and 45-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new ground of rejection.**

In claim 1 and its dependent claims, it is unclear what is encompassed by the term "buffy coat cells". Since the term is not defined in the present application, it is unclear what would constitute or not constitute a buffy coat cell. For example, would any cells, including low-density mononuclear cells, obtained after a Ficoll separation, be

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considered as buffy coat cells? Clarification is requested because the metes and bounds of the claims are not clearly determined.


### ***Conclusion***

#### ***No claims are allowed.***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339 or (571) 272-0776 after January 13, 2004.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, David Guzo, Ph.D., may be reached at (703) 308-1906, or SPE, Irem Yucel, Ph.D., at (703) 305-1998.

Quang Nguyen, Ph.D.

  
DAVID GUZO  
PRIMARY EXAMINER  
8/2/04